

What is Claimed is:

1. An isolated and purified growth factor comprising persephin or fragment thereof or conservatively substituted variant thereof.

2. The isolated and purified growth factor of claim 1 comprising a polypeptide sequence which has at least about 75% sequence identity with SEQ ID NO:79, SEQ ID NO:82 or SEQ ID NO:223 or conservatively substituted variants thereof.

3. The isolated and purified growth factor of claim 2 comprising a polypeptide sequence as set forth in SEQ ID NO:187, SEQ ID NO:198, SEQ ID NO:221 or conservatively substituted variants thereof.

4. The isolated and purified growth factor of claim 3 which promotes survival in mesencephalic cells.

5. An isolated and purified polypeptide comprising:

(a) a pre-pro persephin as set forth in SEQ ID NO:217, SEQ ID NO:185, or SEQ ID NO:196;

(b) a prepro- region of persephin as set forth in SEQ ID NO:218, SEQ ID NO:186, or SEQ ID NO:197;

(c) a pre- region of persephin as set forth in SEQ ID NO:219;

(d) a pro- region of persephin as set forth in SEQ ID NO:220; or

(e) conservatively substituted variants thereof.

6. The isolated and purified growth factor of claim 1 comprising a polypeptide containing a sequence of amino acids having at least about 65% sequence identity with SEQ ID NO:79 or SEQ ID NO:82, or SEQ ID NO:223 wherein the growth factor is from a non-mammalian species.

7. A method for obtaining a neurturin-persephin-GDNF family member growth factor comprising:

(a) isolating (1) from a human genomic or cDNA library, a clone that hybridizes with a polynucleotide

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5 comprising a persephin, neurturin or GDNF sequence or
 fragments thereof or (2) from a human genomic or cDNA
 template, a clone using a polymerase chain reaction
 method with degenerate primers of a conserved region of
 any two of persephin, neurturin or GDNF or fragments of
 10 said conserved regions; and

(b) sequencing said clone.

8. An isolated and purified growth factor that is
 a neurturin-persephin-GDNF family member comprising a
 polypeptide having between about 30% and about 75%
 sequence identity with persephin, between about 30% and
 5 about 75% sequence identity with neurturin and between
 about 30% and about 75% sequence identity with GDNF
 wherein said factor is comprised of a conserved region
 sequence of amino acids having at least a 62.5 percent
 sequence identity with SEQ ID NO:108 or at least a 62.5
 10 percent sequence identity with SEQ ID NO:109 or at least
 a 50 percent sequence identity with SEQ ID NO:110.

9 13. A pan-growth factor comprising a fragment of
 the persephin polypeptide according to claim 1 and a
 fragment of at least one growth factor from the TGF- β
~~superfamily other than persephin.~~

10 14. An isolated and purified nucleic acid molecule
 or nucleic acid molecule complementary thereto comprising
 a nucleotide sequence encoding a growth factor of claim 1
 or a fragment of said nucleotide sequence consisting of
 5 at least 15 contiguous nucleotides.

11 15. The isolated and purified nucleic acid
 molecule or nucleic acid molecule complementary thereto
 of claim 14 comprising a nucleotide sequence encoding a
 persephin polypeptide that promotes survival in
 5 mesencephalic cells wherein said nucleic acid molecule or
 complement thereto specifically hybridizes to SEQ ID
 NO:183, SEQ ID NO:184, SEQ ID NO:194, SEQ ID NO:195, SEQ
 ID NO:199, SEQ ID NO:200, SEQ ID NO:201, or SEQ ID
 NO:202.

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16. The isolated and purified nucleic acid molecule or nucleic acid molecule complementary thereto of claim 15 comprising SEQ ID NO:183, SEQ ID NO:194, SEQ ID NO:199 or SEQ ID NO:201.

13 17. A vector comprising expression regulatory elements operably linked to a nucleic acid molecule of claim 14.¹⁰

14 18. A host cell transformed with the vector of claim 17.¹³

15 19. An isolated and purified nucleic acid molecule comprising:

(a) a pre-pro persephin nucleotide sequence as set forth in SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, or SEQ ID NO:206 or a polynucleotide that specifically hybridizes to SEQ ID NO:179, SEQ ID NO:180, SEQ ID NO:190, SEQ ID NO:191, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, or SEQ ID NO:206;

10 (b) a pre-pro region of a persephin polynucleotide as set forth in SEQ ID NO:181, SEQ ID NO:182, SEQ ID NO:192, SEQ ID NO:193, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, or SEQ ID NO:216;

15 (c) a pre- region of a persephin polynucleotide as set forth in SEQ ID NOS:207, SEQ ID NO:208, SEQ ID NO:209, or SEQ ID NO:210;

(d) a pro- region of a persephin polynucleotide as set forth in SEQ ID NO:211, or SEQ ID NO:212; or

(e) fragment thereof comprising at least 15
20 contiguous nucleotides.

16 20. A recombinant method comprising:

(a) subcloning a polynucleotide encoding the growth factor of claim 1 into an expression vector comprising regulatory elements operably linked to the
5 polynucleotide;

(b) transforming a host cell with the expression vector;

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(c) growing the host cell in a host cell culture;
and

(d) harvesting the growth factor and/or the
~~polynucleotide from the host cell culture.~~

~~17~~ 21. Isolated and purified antibodies which are capable of reacting with a growth factor as defined in claim 1 or an epitope thereof.

~~18~~ 22. A method for detecting the presence of a growth factor in a sample from a patient comprising reacting antibodies according to claim 21 with a growth factor present in the sample and detecting a binding of
5 the antibodies with the growth factor.

~~19~~ 23. A kit for detecting the presence of a growth factor in a sample from a patient comprising antibodies of claim 21 which are capable of detectably reacting with said growth factor, packaged in a container.

~~20~~ 24. A method for preventing or treating cellular degeneration or insufficiency in an individual comprising administering to the individual a therapeutically effective amount of the growth factor of claim 1 or a
5 polynucleotide encoding the growth factor of claim 1.

~~21~~ 25. The method of claim 24 wherein the cellular degeneration or insufficiency is (a) neuronal degeneration resulting from peripheral neuropathy, amyotrophic lateral sclerosis, Alzheimer's disease,
5 Parkinson's disease, Huntington's disease, Ischemic stroke, acute brain injury, acute spinal cord injury, nervous system tumors, multiple sclerosis, or infection; (b) hematopoietic cell degeneration or insufficiency resulting from eosinopenia, basopenia, lymphopenia,
10 monocytopenia, neutropenia, anemias, thrombocytopenia, or stem-cell insufficiencies therefor; or (c) cardiac muscle degeneration or insufficiency resulting from cardiomyopathy or congestive heart failure.

~~22~~ 26. A method for preventing or treating cellular degeneration or insufficiency in an individual comprising

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implanting into the individual, cells that express the growth factor of claim 1.

~~23~~ 27. A method for detecting the presence of a growth factor in a sample from a patient comprising detecting and/or quantitating the presence in the sample of mRNA encoding a growth factor of claim 1.

~~24~~ 28. A method for detecting persephin gene alterations comprising detecting the presence of a non-intact persephin gene in a cell wherein presence of the non-intact gene indicates the presence of gene
5 alterations.

~~25~~ 29. A method for promoting the growth and/or differentiation of a cell in a culture medium comprising adding to the culture medium the growth factor of claim
1.

~~26~~ 30. An isolated and purified persephin antisense polynucleotide comprising a sequence complementary to a nucleic acid sequence of claim 14 and capable of hybridizing to a naturally occurring DNA or mRNA
5 polynucleotide sequence encoding persephin to prevent transcription and/or translation of an encoded persephin polypeptide.

~~27~~ 31. A method for treating a disease condition mediated by expression of persephin by a population of cells comprising administering to said cells an inhibitory effective amount of the antisense
5 polynucleotide of claim 30.

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